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Caprolactam: Condensation of the Carcinogenesis Bioassay Technical Report*

Caprolactam (aminocaproic lactam, 2-oxohexamethylenimine, CAS No. 105-60-2), the monomer used in the production of nylon-6, was selected and testing initiated by the Carcinogenesis Testing Program, National Cancer Institute (now part of the National Institute of Environmental Health Sciences/National Toxicology Program) because nearly one billion pounds per year are produced, because of the widespread use in food packaging materials and clothing, and because no carcinogenicity studies had been done (*1*).

Nylon 6 resins/fibers are used extensively in carpets, knit fabrics, hosiery, thread, hairbrushes, replacement parts for automobiles and machinery, flotation devices, and food packaging. Highly soluble in water, caprolactam reportedly leaches from clothing made from polyamide fibers when soaked in simulated perspiration (*2*). Ferguson and Wheeler (*3*) reported irritation of the skin, eyes, nose, and throat in workers occupationally exposed to caprolactam dust or vapor at concentrations ranging from 10 to 100 ppm.

Methods

Male and female inbred Fischer 344 rats and male and female hybrid B6C3F$_1$ mice, obtained from the Frederick Cancer Research Center, were used in this study. Control and treated groups contained 50 animals of each sex and species. For 103 consecutive weeks all groups received Ralston Purina Laboratory Chow. Treated groups were fed this diet containing 3750 or 7500 ppm (rats) and 7500 or 15,000 ppm (mice) caprolactam (~ 100% pure).

This carcinogenesis bioassay was conducted from January 1977 to February 1979 at Litton Bionetics under a subcontract to Tracor Jitco (prime contractor for the testing program).

All animals that died during the study or that were killed at the end of the exposure period were subjected to a gross necropsy and a complete histopathological examination. Statistical analyses comparing survival and numbers of animals with specific site tumors were done with trend tests and pairwise comparisons (*4-7*). The study design conformed to the NCI Guidelines for carcinogen bioassay (*8*).

Results

Throughout the bioassay, mean body weight gains for treated rats and mice decreased (and dose related) in comparison to controls. For rats, feed consumption by high dose males and females was 70-80% of that for controls; no difference was observed for mice. Survival was comparable among all groups.

The incidences of caprolactam-treated animals with specific site tumors did not differ significantly from those diagnosed in controls. Tables 1 (rats) and 2 (mice) list those primary tumors occurring in at least three animals of any one group.

Discussion

Pituitary carcinomas in male rats showed a statistically significant ($p < 0.05$) positive linear trend (0/46 control, 0/49 low dose, 3/43 high dose); female rat incidences were 2/49, 1/49, 1/47. Comparison of treated groups with controls revealed no statistical difference; likewise when adenomas were combined with carcinomas. This response was not considered associated with caprolactam administration. Other

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Single copies of the complete technical report (TR 214) may be obtained from the Public Information Office, National Toxicology Program, P. O. Box 12233, Research Triangle Park, North Carolina 27709.

Table 1. Primary tumors in male and female F344 rats fed diets containing caprolactam.

Tumor	Males			Females		
	Control	3750 ppm	7500 ppm	Control	3750 ppm	7500 ppm
Adrenal cortical adenoma	1/49	0/50	0/49	4/48	3/50	2/50
Adrenal pheochromocytoma	10/49	8/50	7/49	2/48	5/50	3/50
Hepatocellular carcinoma	1/50	3/49[a]	2/50	0/48	0/50	0/50
Leukemia	13/50	11/50	16/50	9/49	10/50	11/50
Mammary gland	3/50	4/50	1/50	12/49	7/50	7/50
Pituitary adenoma or carcinoma	10/46	11/49	11/47	24/49	24/49	16/47
Subcutaneous fibroma or fibrosarcoma	6/50	4/50	1/50	1/49	0/50	0/50
Testicular interstitial cell	41/49	43/50	48/50	–	–	–
Thyroid C-cell adenoma	3/46	1/45	5/49[b]	2/44	4/46	6/46
Thyroid follicular cell carcinoma	0/46	0/45	0/49	0/44	1/46	2/46[c]
Uterine endometrial stromal polyp	–	–	–	12/49	20/50	15/50

[a]Two other male rats had neoplastic nodules.
[b]One other male rat had a thyroid C-cell carcinoma.
[c]One other female rat had a thyroid follicular-cell adenoma.

Table 2. Primary tumors in male and female $B6C3F_1$ mice fed diets containing caprolactam.

Tumor	Males			Females		
	Control	3750 ppm	7500 ppm	Control	3750 ppm	7500 ppm
Circulatory system hemangiosarcoma	0/50	0/50	0/50	3/50	0/49	1/50
Hepatocellular adenoma	3/50	1/50	4/49	0/50	0/49	1/50
Hepatocellular carcinoma	5/50	9/50	6/49	1/50	1/49	0/50
Leukemia	0/50	0/50	1/50	4/50	2/49	0/50
Lymphoma	9/50	6/50	5/50	17/50	21/49	12/50
Lung alveolar/bronchiolar adenoma	3/50	3/50	2/49	3/50	0/49	0/50
Lung alveolar/bronchiolar carcinoma	1/50	2/50	2/49	0/50	0/49	0/50

effects interpreted as being unrelated to the administration of caprolactam included the negative trends calculated for papillary adenocarcinomas of the mammary gland in female rats (4/49, 1/50, 0/50), for subcutaneous fibromas in male rats (5/50, 3/50, 0/50), for lung alveolar/bronchiolar adenomas in female mice (3/50, 0/49, 0/50), and for leukemias/lymphomas of the hematopoietic system in female mice (4/50, 2/49, 0/50).

Because no evidence of neoplastic or nonneoplastic lesions could be related to dietary administration of caprolactam, under the conditions of this bioassay caprolactam was not carcinogenic for F344 rats or $B6C3F_1$ mice of either sex (*9*).

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